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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,322	12/15/2005	Per Mansson	MANS3010/REF	3648

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BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314-1176

EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,322	MANSSON ET AL.	
	Examiner	Art Unit	
	MELANIE YU	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-18* is/are pending in the application.

4a) Of the above claim(s) *8-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 7 December 2009 have been entered and considered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 1-3, 5, 6, 12, 13 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura et al. (US 2002/0009812) in view of Jacobs et al. (US 6,905,816) further in view of Johnson (US 5,631,172).

Miura et al. teach a coated metal surface on a solid support (thin metal film formed on a prism support, par. 6);

the coating consisting of:

a protein layer firmly attached to the metal surface (BSA, par. 22, 81 and 106) and the protein layer coupled to linker molecules that are bound to low molecular weight antigens (par. 22 and 76; antigens are low molecular weight, par. 41),

wherein the linker molecules are coupled to the protein layer and are bound to the antigen (par. 76 and 105), and

wherein the antigens are reversibly bound to antibodies specific for the antigens wherein the antibodies are more weakly bound to the immobilized antigens than an analyte antigen to be tested (antibodies are bound to antigens on substrate, and are reversibly bound because the antibodies can be displaced during a competition assay and therefore the antibodies are more weakly bound than an analyte because the antibodies can be displaced by the analyte, par. 81).

Miura differs from instant claims in failing to teach the linker specifically having functional end groups attached to the protein and the antigen and the linker between the functional end groups having an aliphatic hydrocarbon chain of 1, 2 or 3 carbon atoms.

Jacobs teaches a protein layer on a substrate surface (BSA coating, col. 16, lines 26-40 and 53-67) comprising linker having functional end groups (NHS-Y-NHS connects amine surface with amine-group containing molecule, col. 17, lines 5-15, Jacobs et al. does not specify with the connecting linker Y is; col. 17, line 47-col. 18, line 7), in order to provide an easy and low cost alternative to providing a number of tests.

And, Johnson teaches a bifunctional linker (spacer arm is bifunctional linker p-Q-r or a-B-c, col. 13, lines 15-22), wherein each bifunctional linker has a linking moiety between the functional end groups wherein the linking moieties have between 0 and 50

carbon atoms, which encompasses the recited range of 1, 2 or 3 carbon atoms (Q and B are linking moieties between the functional end groups, col. 13, lines 32-35) and the linking moiety is alkylene, which is an aliphatic hydrocarbon chain having 2 carbon atoms (Q and B are the linking moieties and may be alkylene, col. 13, lines 42-44), in order to provide a spacer arm for labeling purposes.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include as the linker on the solid support of Miura et al., a bifunctional linker having two functional end groups as taught by Jacobs et al., in order to easily attach an antigen to a substrate having a protein by converting the chemical reactivity of the substrate surface. It would have further been obvious to one having ordinary skill in the art to include as the linking moiety between functional end groups of the bifunctional linker of Miura et al. in view of Jacobs et al., an alkylene which is an aliphatic hydrocarbon chain having 2 carbon atoms as taught by Johnson, because Jacobs et al. does not teach the specific type of linking moiety present between the two functional end groups of a bifunctional linker and is therefore generic with respect to the type of linking moiety that can be incorporated into the bifunctional linker and one would be motivated to use an appropriate linking moiety between functional end groups.

One having ordinary skill in the art would have a reasonable expectation of success when combining Johnson with Miura et al. in view of Jacobs et al. because Jacobs et al. teach a bifunctional linker having end units of aldehydes, carboxylic acids and amine (col. 17, line 47-col. 18, line 7), which are the same bifunctional end groups

taught by Johnson (aldehyde, carboxy, NH_2; col. 17, lines 42-49). Therefore one having ordinary skill would recognize that the linking moiety (alkylene) taught by Johnson is compatible with and can be used to link the two functional end groups of Jacobs et al. to form a linker molecule.

Regarding claims 2 and 18, Miura et al. teach the metal selected from gold, silver, aluminum and nickel (par. 48).

With respect to claims 3, 5 and 15, Miura et al. teach the same antigens bound to the same protein layer (Fig. 13; par. 79 and 80) and the antigen being a narcotic that is cocaine or methamphetamine (par. 41).

Regarding claims 17 and 18, Miura et al. teach the antibody being a monoclonal antibody (BSA is a monoclonal antibody, par. 81) and do not specifically teach how the antibody is produced or the affinity to the antigen. However, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation" Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Since applicant has not disclosed that the specific limitations recited in instant claim 18 is for any particular purpose or solve any stated problem, and the prior art teaches that the affinity of an antibody for an

antigen may be varied depending on the desired affinity required for displacement. Absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures know in the displacement assay art. Although Miura et al. do not teach the specific method of production of the monoclonal antibodies, such a limitation is drawn to a method of making and only the final product must read on the instant claims. The device taught by Miura et al. in view of Jacobs et al. further in view of Tao et al. teach the required product limitations and a monoclonal antibody and therefore reads on the instant claims.

3. Claims 4 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura et al. (US 2002/0009812) in view of Jacobs et al. (US 6,905,816) further in view of Johnson (US 5,631,172), as applied to claims 1 and 12, further in view of Houser et al. (US 2003/0162987).

Miura et al. in view of Jacobs et al. further in view of Tao et al. teach a coated metal surface having a protein layer and an antigen that is a narcotic, but fail to teach the antigen being an explosive.

Houser et al. teach a surface plasmon resonance assay wherein a quartz slide is coated with metal (par. 50) and a sensing film is coated on the metal coated glass slide (par. 16), wherein TNT is the detected antigen (par. 14), in order to provide accurate detection of an explosive in a sample.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include as an antigen in the device of Miura et al. in

view of Jacobs et al. further in view of Johnson, an antigen that is TNT as taught by Houser et al., in order to provide detection of a toxic explosive in a sample (par. 14).

Response to Arguments

1. Applicant's arguments filed 7 December 2009 have been fully considered but they are not persuasive.

2. At pages 7-8, applicant argues that the biological reaction suggested in Miura et al. is a competition reaction and the current invention is concerned with a displacement reaction. Applicant argues that a competition reaction is a variant of a weight gain reaction whereas a displacement reaction is a weight loss reaction and therefore Miura et al. do not read on the instant claims. Applicant further argues that there is no displacement of antibody from the antigen involved in Miura et al., only firm attachment which does not suggest the presently claimed invention.

Applicant's argument is not persuasive because the limitation of a displacement assay is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, even if the limitation of a specific displacement assay were recited in the claims, the claims are drawn to a product and the limitation of performing a displacement assay is drawn to intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is

capable of performing the intended use, then it meets the claim. The claim as rejected only requires that the antigens are reversibly bound to antibodies specific for the antigens, which is taught by Miura et al. as described in the rejection of claim 1 above. Regarding applicant's argument that Miura et al. teach only firm attachment between the antibody and antigen, at paragraph 81, applicant teaches competition between the antigen-antibody reaction immobilized on a substrate and the antibody contained in the sample. The competition causes the antibody contained in the sample to compete with the antibody immobilized to the antigen and therefore teaches a reversible binding between the antigen and the antibody that are initially immobilized to the substrate.

1. At page 9, applicant argues that Miura et al. do not teach a protein layer firmly attached on the metal film as required by the claims, and only teach BSA to produce an immunogen for immunization of mice for production of antibodies.

Applicant's argument is not persuasive because at paragraph 108, Miura et al. describe BSA adhered to a metal film and further in Figure 13 illustrate the BSA attached directly to the metal film. The teaching of Miura et al. at paragraph 43 also coupling an antigen to BSA to serve as a carrier to give an immunogen is not relevant because all embodiments of the invention must be considered.

2. At page 9, applicant argues that Miura et al. do not teach a protein layer coupled to linker molecules as required by the claims, and instead only direct or indirect coupling of antigen by absorption or chemical coupling the antigen to the metal film.

Applicant's argument is not persuasive because Miura et al. teach a protein layer conjugated to an antigen through linker molecules (par. 106, described further below).

The direct or indirect coupling to the metal film taught by Miura et al. is not relevant to the linker molecule used to conjugate the protein layer and antigen.

3. At page 9, applicant argues that Miura et al. fail to disclose a linker molecule at paragraphs 105-110.

Applicant's argument is not persuasive because at paragraph 76, Miura et al. teach conjugation of an antigen (methamphetamine or morphine) conjugated with a protein (BSA) and at paragraphs 105-106 describes the conjugation process which includes mixing the antigen (N-(4-aminobutyl) Nomorphine) with the protein (BSA) with a cross-linker (EDC). Although Miura et al. do not specifically teach EDC being a cross-linker, the prior art recognizes EDC as a known crosslinker as evidenced by Wilkie et al. (US 2002/0022588) at paragraph 316. Therefore, contrary to applicant's arguments, Miura et al. teach a linker molecule at paragraph 106.

4. At pages 9-10, applicant argues that Miura et al. do not teach displacement of an antibody anywhere in the disclosure.

Applicant's argument is not persuasive because the claim only requires reversible binding between the antigen and the antibody. The antibody in the sample competes with the antibody conjugated to the BSA on the substrate. Therefore Miura et al. teach that the binding between the antibody conjugated to the BSA is reversible.

5. At page 10, applicant argues that Jacobs do not teach a displacement reaction.

Applicant's argument is not persuasive because Jacobs is not relied upon for teaching a displacement reaction and the claim only requires reversible binding

between the antibodies and antigens. Additionally, Miura et al. is relied upon for teaching the reversible antibody-antigen binding.

6. At page 10, applicant argues that that Johnson fails to teach what kind of linkers between a protein layer on a solid support and a low-molecular weight antigen would be suitable for immunoassays where antibodies reversibly bind to antigens that are dissociated and displaced by sample antigens.

Applicant's argument is not persuasive because Johnson is relied upon only for teaching the linking moiety between two functional end groups having the required number of carbon atoms, and is not relied upon for teaching the entire bifunctional linker that is present between a protein layer and a low-molecular weight antigen. Jacobs is relied upon for teaching a bifunctional linker and only does not teach the connecting linker between the functional end groups.

7. At page 11, applicant argues that the present invention shows unexpected results that only shorter aliphatic chains of less than 4 carbon atoms produces unexpected results of a significant displacement of antibody upon exposure to the analyte.

Applicant's argument is not persuasive, firstly because the claim does not require displacement of an antibody upon exposure to the analyte and only requires the antigens to be reversibly bound to the antibodies. Secondly, applicant's argument is not persuasive because the specification provides no comparison or evidence that shows that an aliphatic hydrocarbon chain having more than 3 carbon atoms provides both unexpected and unobvious benefits. The mere conclusion in the specification that an

aliphatic hydrocarbon chain having less than 4 carbon atoms is beneficial in displacement is not sufficient to show unexpected results. MPEP 716.02(b).

Conclusion

3. No claims are allowed.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELANIE YU whose telephone number is (571)272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Melanie Yu/
Primary Examiner, Art Unit 1641